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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,941	09/24/2003	David A. Brake	15471ZYZ (PC9590F)	4787

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Dr. Peter C. Richardson
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EXAMINER

PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 09/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/669,941

Applicant(s)

BRAKE ET AL.

Examiner

Ginny Portner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-9 and 11-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-4, 6-9, 11-20, 22-24, 26-32 is/are rejected.
- 7) ☐ Claim(s) 21, 25 and 28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

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DETAILED ACTION

Claims 1-2, 6-7, 14, 18, 24-25 and 32 have been amended; claims 1-4, 6-9, 11-32 are pending.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Allowable Subject Matter

2. Claims 21,25 and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Objections/Rejections Withdrawn

3. Claim 24 objected to because of the following informalities has been obviated in light of the amendment of claim 24 to positively recite the essential/critical components for inducing a protective immune response.

4. Claims 2,7,18 and 25 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been obviated by amendment of the claims to recite the presence of a structural difference defined by a functional recitation supported by the disclosure in the instant Specification.

5. Claims 1-4,6-9,11-12, 13-20,22-27,29-32 rejected under 35 U.S.C. 112, first paragraph, (scope) is herein withdrawn in light of Applicant's traversal.

Rejections Maintained

6. Claim 32 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained for reasons of record in paper number 252004, paragraph 6.

7. Claims 1,6,11-12, 24, 30-31 and 32 rejected under 35 U.S.C. 102(e) as being anticipated by Conrad et al (US Pat. 5,707,617), for reasons of record in paper number 252004, paragraph 9.

8. Claims 1,3-4, 6, 8-9, 13, 15-16, 17, 19-20 and 32 rejected under 35 U.S.C. 102(b) as being anticipated by Lindsay et al (Am. J. Vet. Res., Vol. 56, pages 1176-1180, Sept. 1995), is maintained for reasons of record in paper number 252004, paragraph 10.

9. Claims 1-3, 6-8, 13-15, 17-19 are rejected under 35 U.S.C. 102(a) as being anticipated by Lindsay et al (different inventive entity, January 1996), is maintained for reasons of record in paper number 252004, paragraph 11.

10. Claims 1,3-4, 6, 8-9 rejected under 35 U.S.C. 102(a) as being anticipated by Hemphill et al (October 1996), is maintained for reasons of record in paper number 252004, paragraph 12.

11. Claims 1, 6, 13 and 17 rejected under 35 U.S.C. 102(e) as being anticipated by Kim et al (US Pat. 5,976,553), is maintained for reasons of record in paper number 252004, paragraph 13.

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12. Claims 1-4 and 6-9 remain rejected under the judicially created doctrine of obviousness type double patenting over claims 1-8 of US Patent No 6,656,479 for reasons of record in paper number 252004, and the fact that an effective terminal disclaimer was not submitted in response to the Office Action.

Response to Arguments

13. The rejection of claim 32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is traversed on the grounds that:

- a. Claim 32 has been amended to recite the phrase “one or more antigens other than a Neospora antigen” to clarify what is being claimed.

14. It is the position of the examiner that the issue raised was with respect to the presence of “;” semicolons, to define three different combination vaccines, each invention being separated and defined as a different invention through being set off by the presence of “;” in two different places in the claim. The semi-colons have not been removed. The invention is still not distinctly claimed as what veterinary acceptable carriers would serve as a combination vaccine has not been defined. Removal of the semicolons from the claim could obviate this rejection.

15. The rejection of claims 1,6,11-12, 24, 30-31 and 32 under 35 U.S.C. 102(e) as being anticipated by Conrad et al (US Pat. 5,707,617), is traversed on the grounds that:

- b. Conrad “is primarily directed to two pathogenic bovine strains of Neospora”.

16. It is the position of the examiner that Conrad formulated and immunized with “culture-derived” tachyzoites of the Neospora isolates (see col. 28, lines 3-6), which is one of the modes disclosed in Applicant’s Specification for the attainment of an attenuated strain of Neospora.

17. Conrad et al is additionally asserted to not “teach or suggest attenuated strains derived from these pathogenic isolates.”

18. Contrary to Applicant’s assertions, Conrad does disclose derived cultures of isolated Neospora (see col. 28, line 6), and does teach the importance of attenuated Neospora vaccine compositions (see col. 11, lines 35-36 and lines 45-47). The derived isolated Neospora culture cells were obtained through culturing the isolated to obtain “culture derived” tachyzoites.

Conrad et al does disclose the instantly claimed invention which includes within its definition culture derived cultures of isolated Neospora cells.

Arguments directed to temperature sensitive attenuated strains, it is the position of the examiner that Conrad is no longer applied to the dependent claims that set forth is embodiment. All cells are temperature sensitive, but the type of temperature sensitivity newly submitted and encompassed by amended claims 2, 7, 14, 18 and 25 is not anticipated by Conrad et al.

19. The rejection of claims 1, 3-4, 6, 8-9, 13, 15-16, 17, 19-20 and 32 under 35 U.S.C. 102(b) as being anticipated by Lindsay et al (Am. J. Vet. Res., Vol. 56, pages 1176-1180, Sept. 1995) is traversed on the grounds that:

c. “there is no teaching in Lindsay et al that the cultures exhibit attenuated pathogenicity as compared to the parent pathogenic *N. caninum* strain.

20. It is the position of the examiner, while Lindsay et al does not use the word “attenuated” in the article, the reference meets the definition of an attenuated stain of *N. caninum* provided by Applicant’s Specification at page 5, lines 17-27, specifically, “high serial passage”. The laboratory strains of *N. caninum* were NC-1, NC-2 and NC-3, and were maintained in culture by

serial passage, and over time became high serial passage laboratory strains of *N. caninum* (see page 1179, col. 2, Discussion section, paragraph 3). Each strain of *N. caninum* designated as NC-1, NC-2 and NC-3 presented as differing strains that were distinguishable one from the other.

21. Lindsay et al is further traversed on the grounds that the reference: Does not teach or suggest an isolated strain that exhibits attenuated pathogenicity or how to obtain such a strain.

22. It is the position of the examiner that all of the strains of *N. caninum* were isolated from the host animal in which they cause pathogenic disease, and maintained in a culture of cells. The claimed invention is directed to a "culture of cells" of an isolated strain derived from a pathogenic parent strain of a species of *Neospora*, and the strains of Lindsay et al meet the definition of an attenuated strain of *Neospora caninum* provided by Applicant, the strain was isolated from and derived from a pathogenic strain of *Neospora caninum* by high serial passage.

23. Applicant states that "It is true that attenuation of a pathogenic *Neospora* parent strain can be achieved by in vitro passaging."

24. The examiner thanks Applicant's representative for supporting the application of Lindsay et al against the claims by making statements on the record that serial passaged strains *N. caninum* comprise attenuated strains derived from the parent strain, and comprise various attenuated cells derived from the parent strain. Applicant's arguments directed to a homogenous strain of attenuated *Neospora* is not commensurate in scope with the instantly claimed invention. The recitation of the term "an isolated strain" in the claims is not limited to any strain that is a single cell type but is being read to include a culture of cells that is a heterogeneous culture of cells that is isolated from the native host animal. Lindsay et al still reads on the claimed

invention which has been amended to recite the phrase "an isolated strain", because all of the strains of Lindsay et al were isolated from the native host animal, and maintained as a culture of cells which were derived by serial passage in cultures, of the several methods defined for attaining an attenuated strain of *N.caninum*.

25. The rejection of claims 1-3, 6-8, 13-15, 17-19 under 35 U.S.C. 102(a) as being anticipated by Lindsay et al (different inventive entity, January 1996) is traversed on the grounds that:

- d. The reference does not disclose an isolated, attenuated strain derived from a pathogenic parent strain of a species of *Neospora* as presently claimed.
- 1. It is the position of the examiner that Lindsay et al discloses mutated strains of *Neospora caninum* that were produced with the same chemical mutagen used by Applicant to introduce and produce mutant strains of *Neospora caninum*. The mutant strains were maintained/attenuated through subculturing in vitro and also evidenced genetic changes due to chemical mutations. The mutant, derived strains of *Neospora caninum* are attenuated based upon Applicant's own definition of attenuated found at page 5, lines 17-20. No evidences has been provided to show that the mutant strains of Lindsay et al are not temperature sensitive, and that mutant strains produced using the same method of Lindsay et al does not produce temperature sensitive mutant strains of *Neospora*.
- 1 Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594

2. The characteristics of the strains are not discussed, but by all comparable data, the strains of Lindsay et al are the same or equivalent strains now claimed. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. "The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

Inherently the reference anticipates the instantly claimed invention.

26. The rejection of claims 1,3-4, 6, 8-9 under 35 U.S.C. 102(a) as being anticipated by Hemphill et al (October 1996 , is traversed on the grounds that:

e. The strains of *Neospora caninum* of Hemphill are not isolated attenuated strains.

27. It is the position of the examiner that all of the in vitro strains of Hemphill were isolated and identified as *Neospora caninum* and maintained as viable strain through subculuring into a culture of cells of an isolated *Neospora caninum*. The reference still anticipates the instantly claimed invention.

28. The rejection of claims 1, 6, 13 and 17 under 35 U.S.C. 102(e) as being anticipated by Kim et al (US Pat. 5,976,553) is traversed on the grounds that:

f. The transformed strain is not necessarily attenuated in its pathogenicity as compared to the parent strain.

29. It is the position of the examiner that Kim et al disclose attenuated parasites, specifically attenuated parasites constructed by generating deletions of target parasite genes that disable the parasite in a selected capacity using the methods of the present invention and the constructive reduction to practice of attenuated pathogenic strains of parasite is disclosed for *Neospora* (Kim

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et al, claim 4). Kim et al teaches the deletion of target genes include those involved in the biosynthesis of key metabolites. The growth patterns of the attenuated parasite relative to the parent strain would differ because the attenuated parasite would not grow in the absence of a supplemental metabolite; the growth would stop in the absence of the needed metabolite. An example of immunogenic strain is an attenuated parasite to be used as a vaccine to generate antibodies against the expressed sexual phase antigens, wherein the parasite is incapable of switching into the sexual stage, since it also carries a deletion in genes required for the switch. Applicant asserts that “One skilled in the art would not reasonably expect that the teachings provided by Kim et al with respect to attenuating Toxoplasma would be successfully applied to Neospora”. It is the position of the examiner that while Toxoplasma was exemplified, Kim et al provides guidance and teaching for introducing deletions in genes for attenuating parasites to include Neospora (see Kim et al claims), and claims a transformed Neospora parasite that comprises heterologous DNA . At the time of filing of the instant Specification and the filing of the Kim et al Application (May 16, 1996), genes for Neospora were known in the art that could be used to attenuate Neospora strains :

- g. 14-3-3 gene (Mol. Biochem Parasitol., 1996).
- h. Dense granule protein 1 & 2 (Clin. Diagn. Lab. Immunol., 1996)
- i. Major surface protein, Nc-p43 (Parasitology Res., 1996; Infection Immun. (1996).

Kim et al is not applied against claims directed to temperature sensitive strains with a reduced growth rate as currently amended, but does disclose an attenuated Neospora strain and a modified strain, modified with a modifying agent, specifically exogenous DNA (see claims).

New Grounds of Objections and Rejection

Claim Objections

30. Claim 12 is objected to because of the following informalities: Claim 12 recites the misspelled term “ail” which should be ---oil----. Appropriate correction is required.

Claim Rejections - 35 USC § 102

31. Claims 17,22,23, 24, 26-27, 29-30', 31, 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Conrad et al (US Pat. 6,716,423). Conrad et al claim a method of making a vaccine and a method of vaccinating a mammal against neosporosis, the method of vaccinating comprising the step of :

Administering to the mammal an immunologically effective amount of vaccine and a veterinarily acceptable carrier, wherein the vaccine comprises live cells of an isolated strain derived from a pathogenic parent strain of a species of Neospora (see Conrad et al, claims 1-15, especially claims 4 and 9; "cultures of BPA1 and BPA2 isolates had been maintained with continuous growth for 10 and 6 months, respectively (col. 21, lines 17-29") and also disclose Neospora caninum strain NC-1 (col. 1, lines 23-28) which was maintained in culture and sub-cultured every 2-3 days.

The mammal is taught to include cattle, sheep, goats or other animals infected by Neospora (see col. 15, lines 4-10).

The vaccine compositions were combined with an immunologically effective amount of cells together with a carrier such as water, saline or buffered vehicles and various adjuvants which include oil-in-water emulsions, bacterial endotoxin, Bordetella pertussis (see col. 15, lines 25-63).

Conclusion

32. This is a non-final action.
33. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Lindsay et al (Feb 1999) is cited to show NCts-4 and NCts-12 to be strains of attenuated Neospora that reverted to wild-type strains when administered to an animal..
34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
August 17, 2004

L. R. F. Smith
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